

WHAT IS CLAIMED IS:

1 1. A nucleic acid molecule comprising an aptamer and a polynucleotide
2 that encodes a transcriptional regulatory polypeptide, wherein binding of a ligand to the
3 aptamer inhibits translation of the transcriptional regulatory polypeptide.

1 2. The nucleic acid of claim 1, wherein the ligand is a cell-permeable
2 small organic molecule.

1 3. The nucleic acid of claim 2, wherein the ligand is Hoechst dye 33258.

1 4. The nucleic acid of claim 1, wherein the ligand is a metal ion.

1 5. The nucleic acid of claim 1, wherein the ligand is an antibiotic.

1 6. The nucleic acid of claim 1, wherein the ligand is a steroid.

1 7. The nucleic acid of claim 1, wherein the transcriptional regulatory
2 polypeptide is a repressor.

1 8. The nucleic acid of claim 1, wherein the transcriptional regulatory
2 polypeptide is a transcriptional activator.

1 9. The nucleic acid of claim 1, wherein the transcriptional regulatory
2 polypeptide is a coactivator.

1 10. The nucleic acid of claim 1, wherein the transcriptional regulatory
2 polypeptide comprises a DNA-binding domain.

1 11. The nucleic acid of claim 10, wherein the DNA-binding domain is
2 that of a protein selected from the group consisting of E2F-1, GAL4, a STAT protein, a
3 steroid/thyroid receptor protein, a Cys2-His2 zinc finger DNA binding motif, and a
4 tetracycline repressor.

1 12. The nucleic acid of claim 1, wherein the transcriptional regulatory
2 polypeptide comprises a transcriptional repressor domain.

1 13. The nucleic acid of claim 12, wherein the transcriptional repressor
2 domain is that of a protein selected from the group consisting of Rb protein, v-erbA, retinoic

3 acid receptor alpha, thyroid hormone receptor alpha, yeast Ssn6/Tup1 protein complex,
4 SIR1, NeP1, TSF3, SFI, WT1, Oct-2.1, E4BP4, KRAB and ZF5.

1 14. The nucleic acid of claim 12, wherein the transcriptional repressor
2 domain is that of p53.

1 15. The nucleic acid of claim 1, wherein the transcriptional regulatory
2 polypeptide comprises a transcriptional activation domain.

1 16. The nucleic acid of claim 1, wherein the nucleic acid is an mRNA
2 molecule.

1 17. The nucleic of claim 16, wherein the mRNA is bound to a ligand.

1 18. An expression cassette that comprises a promoter operably linked to a
2 polynucleotide from which is transcribed the nucleic acid of claim 1.

1 19. An expression vector that comprises the expression cassette of
2 claim 18.

1 20. The expression vector of claim 19, wherein the expression vector is a
2 viral vector.

1 21. The expression vector of claim 20, wherein the viral vector is selected
2 from the group consisting of an adenoviral vector, a retroviral vector, and an adeno-
3 associated viral vector.

1 22. The expression vector of claim 19, wherein the expression vector is a
2 nonviral vector.

1 23. The expression vector of claim 19, wherein the expression vector
2 further comprises a second polynucleotide, wherein transcription of the second
3 polynucleotide is regulated by the transcriptional regulatory polypeptide.

1 24. The expression vector of claim 23, wherein the second polynucleotide
2 encodes a therapeutic polypeptide.

1 25. The expression vector of claim 23, wherein the second polynucleotide
2 is operably linked to a binding site for the transcriptional regulatory polypeptide.

1 26. A cell that comprises the nucleic acid molecule of claim 1.

1 27. The cell of claim 26, wherein the cell further comprises a second
2 polynucleotide, wherein transcription of the second polynucleotide is regulated by the
3 transcriptional regulatory polypeptide.

1 28. The cell of claim 27, wherein the second polynucleotide is included in
2 the nucleic acid.

1 29. The cell of claim 27, wherein transcription of the second
2 polynucleotide yields an antisense nucleic acid.

1 30. The cell of claim 27, wherein the second polynucleotide encodes a
2 polypeptide.

1 31. The cell of claim 30, wherein the polypeptide is a therapeutic
2 polypeptide.

1 32. The cell of claim 31, wherein the therapeutic polypeptide is selected
2 from the group consisting of a toxin, a cytokine, a kinase, a phosphatase, a transcriptional
3 regulatory protein, an antibody, and a tumor suppressor.

1 33. The cell of claim 32, wherein the polypeptide is a tumor suppressor.

1 34. The cell of claim 33, wherein the tumor suppressor is p53.

1 35. The cell of claim 26, wherein the cell further comprises a ligand that
2 binds to the aptamer.

1 36. A method of regulating expression of a gene, the method comprising:
2 contacting with an aptamer-binding ligand an RNA that comprises an aptamer
3 and a polynucleotide that encodes a transcriptional regulatory polypeptide that regulates
4 expression of the gene;

5 wherein the ligand binds to the aptamer, thus inhibiting translation of the
6 transcriptional regulatory polypeptide resulting in a change in the expression level of the
7 gene.

1 37. The method of claim 36, wherein the change in the expression level of
2 the gene is proportional to the amount of aptamer-binding ligand administered.

1 38. The method of claim 36, wherein the transcriptional regulatory
2 polypeptide is a repressor, whereby binding of the ligand to the aptamer inhibits translation
3 of the repressor thus causing an increase in the expression level of the gene.

1 39. The method of claim 36, wherein the transcriptional regulatory
2 polypeptide is a transcriptional activator, whereby binding of the ligand to the aptamer
3 inhibits translation of the transcriptional activator thus causing a decrease in the expression
4 level of the gene.

1 40. The method of claim 36, wherein the gene comprises a binding site for
2 the transcriptional regulatory polypeptide.

1 41. The method of claim 36, wherein the gene is included in a
2 chromosome.

1 42. The method of claim 36, wherein the gene is extrachromosomal.

1 43. The method of claim 36, wherein the mRNA is contained in a cell.

1 44. The method of claim 43, wherein the cell is part of a multicellular
2 organism.

1 45. The method of claim 44, wherein the contacting is accomplished by
2 administering the ligand to the organism.

1 46. The method of claim 36, wherein the RNA is transcribed from an
2 expression cassette that comprises a promoter operably linked to a polynucleotide from
3 which is transcribed the RNA.

1 47. The method of claim 46, wherein the promoter is a constitutive
2 promoter.

1 48. A method of retarding undesirable cell proliferation, the method
2 comprising administering to undesirably proliferating cells:
3 a nucleic acid construct that comprises a promoter operably linked to a
4 polynucleotide, wherein the polynucleotide is transcribed to yield an mRNA that comprises
5 an aptamer and a polynucleotide sequence that encodes a transcriptional regulatory
6 polypeptide that regulates expression of a gene involved in regulation of cell proliferation;
7 an aptamer-binding ligand that binds to the aptamer;
8 wherein the binding of the ligand to the aptamer inhibits translation of the
9 transcriptional regulatory polypeptide, thus causing a change in the expression level of the
10 gene, which change in expression level ameliorates the undesirable cell proliferation.

1 49. The method of claim 48, wherein the gene involved in regulation of
2 cell proliferation is a tumor suppressor gene and the transcriptional regulatory polypeptide is
3 a repressor, whereby binding of the ligand to the aptamer results in an increase in the tumor
4 suppressor gene expression level.

1 50. The method of claim 48, wherein the gene involved in regulation of
2 cell proliferation is a transgene.

1 51. The method of claim 50, wherein the gene comprises a promoter
2 operably linked to a polynucleotide that encodes a polypeptide involved in regulation of cell
3 proliferation.

1 52. The method of claim 51, wherein the promoter is a constitutive
2 promoter.

1 53. The method of claim 50, wherein the gene is included on an
2 expression vector that is administered to the undesirably proliferating cells.

1 54. The method of claim 53, wherein the expression vector further
2 comprises the nucleic acid construct.

1 55. The method of claim 48, wherein the nucleic acid construct is
2 included on an expression vector that is administered to the undesirably proliferating cells.